

Application No.: 10/594,256

Docket No.: JCLA21973

**REMARKS****Present Status of the Application**

The First Office Action dated June 12, 2008 objected the specification, claims 15-16 and the sequence listing for informalities. Claims 9-16 were rejected under 35 U.S.C. 112, first paragraph as failing to comply with the enablement requirement.

Claim 9 has been amended for clarification, while claims 11, 13 and 15 have been amended for correcting informalities and correcting dependency. The specification has been amended for correcting informalities and for clarification purposes. It is believed that the amendments are supported by the original specification and drawings of this application and can overcome the objections. After entering the amendments and considering the following discussions, a notice of allowance is respectfully solicited.

**Discussion for the objections**

The specification was objected as containing embedded hyperlink of browser-executable form.

The specification has been amended to remove the hyperlink (the underline) of the website.

The sequence listings were objected under 37 CFR 1.821 through 1.825 for not identifying the sequences in the specification (page 15) with SEQ ID NO identifications. Also, no letter stating that the submitted sequence listing in paper format and computer readable format are the same is submitted.

The specification (3<sup>rd</sup>-5<sup>th</sup> paragraphs of page 15) has been amended to identify the sequences appropriately by SEQ ID NOs. Entry of the above amendments is respectfully requested.

Claims 15-16 were objected for typological errors.

Claim 15 has been amended to correct the typological errors.

Entry of the amendments to the specification and claims is respectfully requested.

Application No.: 10/594,256

Docket No.: JCLA21973

**Response to Notice to Comply**

In response to Notice to Comply, the specification has been amended to provide SEQ ID Nos for sequence present on page 15.

The undersigned hereby state that the contents of the paper and computer readable copies of the "Sequence Listing" filed on September 25, 2006 are the same and include no new matter.

A copy of the notice to Comply is attached hereto.

**Discussion of 112 rejections**

*Claims 9-16 were rejected under 35 U.S.C. 112, first paragraph as failing to comply with the enablement requirement.*

The Office Action is of the opinion that the specification only provides a single working example regarding NOD2/CARD15 polymorphisms in patients at risk for graft vs host disease after undergoing allogenic stem cell transplantation.

Claim 9 has been amended to be limited to the prognosis and/or diagnosis of "rejection responses occurring after transplantation, graft versus host disease, and/or host versus graft disease".

Applicants believe that the data presented in the present application clearly demonstrates an increased risk for the claimed conditions in patients carrying one of the claimed polymorphisms. Moreover, the stem cell transplantation data presented in the present application is one model for observing transplantation rejection responses and therefore predictive for transplantation rejection responses in other types of transplantations.

The Office Action further considered that the description provided in the application was not sufficient, and cited *Holler* (D1) and *Granell* (D2) for showing the unpredictability concerning the use of NOD2/CARD15 mutations for the prognosis of graft vs host disease after stem cell transplantation, along with *Brenmoehl* (D3) for showing the unpredictability concerning the use of NOD2/CARD15 mutations for the prognosis of sepsis.

Application No.: 10/594,256

Docket No.: JCLA21973

Regarding the unpredictability of the art in this field, Applicant would like to point out that the claimed method is just one useful indicator for the prediction of rejection responses occurring after transplantation, graft versus host disease, and/or host versus graft disease and that the claimed method does not have to answer all outstanding questions in this field of medicine to be usable by a skilled practitioner.

The *Holler* (D1) publication in fact confirms the findings as demonstrated in the present application regarding rejection responses occurring after transplantation, graft versus host disease, and/or host versus graft disease (see page 4191, col. 1, 1st paragraph) as all results presented in Table 3 of *Holler* are considered to be statistically significant. *Holler* also state on page 4192, col. 1, 2<sup>nd</sup> paragraph that even after analysis of differences between different cohorts that: NOD2/CARD15 remained a significant risk factor for GvHD and overall TRM in the subgroups.”.

As for the discussion in *Holler* about the effect of gastrointestinal decontamination on the predictive strength of the NOD2/CARD15 polymorphisms, Applicants would like to point out that this should not be cited as relevant to the enablement requirement of the claimed invention. If this was the case, any medical diagnostic/prognostic method or medical treatment would need to demonstrate its effect under all possible clinical treatment scenarios and this is just not practicable. Also any medical practitioner is of course aware that any particular treatment may have an influence on the effectiveness of a diagnostic/prognostic method or on the effect of another treatment.

In response to the *Granell* (D2) publication, the same rationale identical to the above paragraph is applicable. Again a further treatment has been carried out and any medical practitioner would be aware that destroying the T cells of the donor sample may have an influence on the effectiveness of a diagnostic/prognostic method or on the effect of another treatment.

In response to the *Brenmoehl* (D3) publication, this publication is directed to sepsis related mortality, and the related disease has been cancelled from the amended claim 9. Therefore this publication is no longer relevant.

Accordingly, withdrawal and reconsideration of these 112 rejections are respectfully

Application No.: 10/594,256

Docket No.: JCLA21973

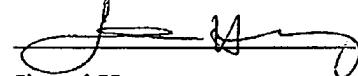
requested.

**CONCLUSION**

For at least the foregoing reasons, it is believed that the pending claims 9-16 of the present application patently defines over the prior art and are in proper condition for allowance. If the Examiner believes that a telephone conference would expedite the examination of the above-identified patent application, the Examiner is invited to call the undersigned.

Respectfully submitted,  
J.C. PATENTS

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Jiawei Huang  
Registration No.: 43,330

4, Venture Suite 250  
Irvine, CA. 92618  
Tel: (949) 660-0761  
Fax: (949) 660-0809